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Hypothyroidism and Infectious Mononucleosis—An Unusual Association

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INFECTIOUS MONONUCLEOSIS is a generalized disease. Extensive biopsy and autopsy studies indicate there are as many lesions of infectious mononucleosis as there are organs and tissues in the body.^{1,2,8} Although it is considered a rare complication, hypothyroidism has been known to follow acute and subacute thyroiditis. In 1961 Mosonyi and Rusvai⁷ reported the findings in two patients in whom acute and subacute thyroiditis developed as a complication of infectious mononucleosis. Masked thyroiditis resulting in varying degrees of hypothyroidism may be a more frequent complication of this disease than is generally believed. It could in an occasional patient account for such

frequently debilitating symptoms as general malaise, weakness and mental depression which may last for weeks, months and, in some cases, a year or more following an attack of acute infectious mononucleosis.

The purpose of this paper is to report a single case in which the relationship of hypothyroidism and infectious mononucleosis appears more than accidental. In this patient classical hypothyroidism, including myxedema heart, developed.

Report of a Case

A 29-year-old Caucasian male graduate student with no previous history of serious illnesses was seen in the Student Health Service in September 1964 with a history of fatigue, malaise and cervical adenopathy of three weeks' duration. A blood count revealed lymphocytosis with 14 per cent atypical lymphocytes. Heterophile agglutination was 1:1792 or greater. A diagnosis of infectious mononucleosis was made.

In October 1964, because of persistent symptoms, the patient was admitted to hospital. Serum creatinine was elevated to 1.5 mg per 100 ml with creatinine clearance of 90.8 ml per minute. There was no albumin or sugar in a 24-hour specimen of urine. No abnormalities were noted in liver studies. In an x-ray film of the chest, the heart size appeared to be within normal limits (Figure 1). Although there was little improvement, the patient was discharged after five days to convalesce at home.

In November 1964 he was readmitted to hospital because of continued fatigue and malaise and

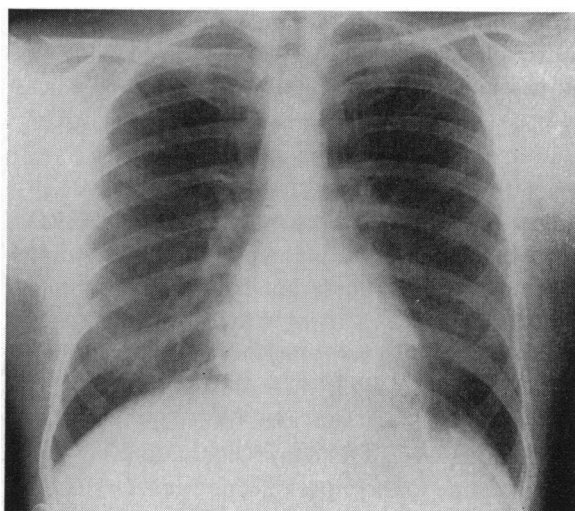


Figure 1.—X-ray film, taken in October 1964, showing size of heart within normal limits.

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new symptoms of muscle twitching, lateral chest pains, muscle stiffness, headache, nausea and questionable facial and submandibular puffiness and periorbital edema, mild chills and fever.

He appeared chronically ill and his complexion was sallow. There was slightly submandibular swelling.

The heterophile was 1:896. An x-ray film was considered unchanged. He was considered to be hypochondriacal and was treated with Librium® for the anxiety state and with multivitamins. After 14 days he was discharged with a diagnosis of chronic infectious mononucleosis.

In December 1964 he entered the hospital for the third time with nonspecific complaints of nausea, "black stool," aching in the lower abdomen and suprapubic area unrelated to meals, and persistent malaise.

As before, his complexion was sallow. Enlargement of a submandibular gland was noted.

Results of blood chemical determinations were within normal limits. An x-ray film of the chest showed a 2 cm increase in the transverse diameter of the heart in comparison with the previous film. This was attributed to failure to take a full inspiration. Hypomotility of the bowel was suggested in an upper gastrointestinal x-ray study. The patient was discharged after five days with a diagnosis of psychoneurosis manifested by asthenia and musculoskeletal symptoms.

Between January 1965 and June 1966 he was not seen by us, but a personal physician who saw him once during that time found him to be anemic and prescribed supplemental iron.

In July 1966, in a routine pre-employment physical examination, an enlarged cardiac silhouette was noted. The patient was referred to his personal physician, who confirmed the cardiac enlargement and suggested that there might be pericardial effusion. He was then referred to the Student Health Service for further evaluation and, on review of the x-ray film he brought with him (Figure 2), the finding of an enlarged flask-shaped heart was strongly suggestive of "myxedema heart," first reported by Zondek¹⁰ and later classically described by Fahr.³ Protein-bound iodine was 1.0 mcg per 100 ml of serum.

The patient was admitted to hospital for the fourth time with a diagnosis now of hypothyroidism and myxedema heart.

The symptoms and signs were classical for hypothyroidism—increasing dryness of skin, intoler-

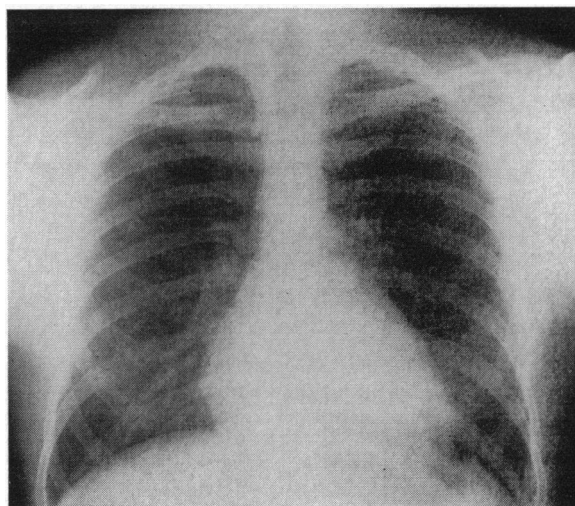


Figure 2.—Enlargement and "flask shape" of heart shown on film taken in July 1966.

ance to cold, yellowness of skin, coarseness of hair, deepening of voice, facial puffiness, increased fatigability and mild shortness of breath, difficulty in completing studies, and tendency to be less physically active.

Hemoglobin was 12.7 gm per 100 ml of blood, the mean corpuscular hemoglobin 33, mean corpuscular hemoglobin concentration 33 and mean corpuscular volume 102. Results of urinalysis were within normal limits. Serum carotene was 830 (normal 250) and serum cholesterol 305 mg per 100 ml. An electrocardiogram showed sinus bradycardia, low QRS voltage. Increased transverse diameter of the heart was noted on an x-ray film of the chest. Radioactive iodine uptake was 1.6 percent at six hours and 2.4 percent at 24 hours. The red corpuscle uptake of T_1 was 21 percent (normal 25-35 percent). PBI was 0.8 percent. A test for antithyroid antibodies was positive in a 1:10 dilution.

Thyroid replacement therapy was begun, and over the next three months the patient made dramatic recovery from the hypothyroid state, and the heart size returned to normal (Figure 3).

Discussion

The symptoms and signs in the case here reported closely parallel those of subacute thyroiditis, but clearly also those of chronic infectious mononucleosis. The fact that the patient had severe infectious mononucleosis with probable renal involvement made it difficult to diagnose the concurrent symptoms of subacute thyroiditis and the early symptoms and signs of hypothyroidism.⁵

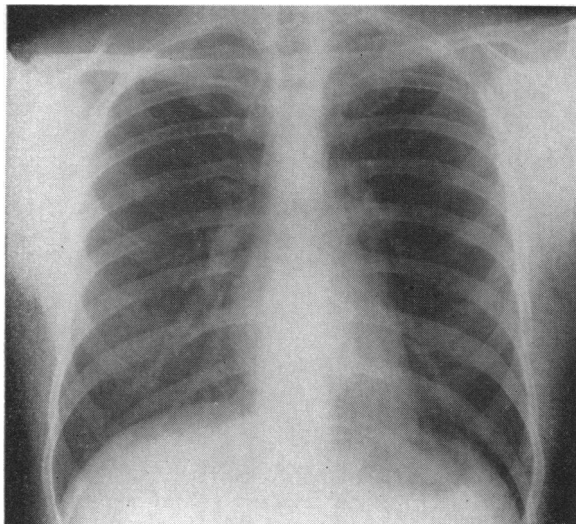


Figure 3.—Film taken after thyroid replacement therapy shows heart size back to normal.

Acute and subacute thyroiditis may be asymptomatic except for swelling and tenderness of the thyroid gland, although even this may be absent or so mild that it is overlooked. The onset of the disease may be insidious in nature, with the patient first noticing a "sore throat" and fatigability. These vague symptoms may last from two weeks on the average to as long as two to three months or more in 25 percent of the patients.⁹ The classic symptoms include fever, a feeling of chilliness, generalized headache, night sweats, malaise, nausea, vomiting, cough, loss of weight and musculoskeletal pains. As can be seen, therefore, these symptoms may be also applicable for an upper respiratory infection as well as infectious mononucleosis. Mistaken diagnosis has been reported.^{4,6} The variety of symptoms is related to the multiple organ involvement of infectious mononucleosis.

Thyroid involvement by infectious mononucleosis may be more frequent than is generally believed. Usually thyroiditis has a self-limiting course with no serious complications, and often is so mild that the diagnosis may be overlooked. The single case presented here seems to indicate a rather close relationship—more than an accidental association—between thyroid involvement and infectious

mononucleosis. It is suggested that subacute thyroiditis or hypothyroidism be included in the differential diagnosis of a protracted course of infectious mononucleosis, for the symptoms of the former two diseases can be masked by the latter.

Summary

A patient with infectious mononucleosis had continuing symptoms several months after the acute phase of the disease. He appeared chronically ill, had a sallow complexion, easy fatigability, muscle twitching and stiffness, thoracic pain, headache, nausea, chills, fever and questionable facial and mandibular puffiness. He was thought to have chronic infectious mononucleosis and to be hypochondriacal.

A year and a half later, when cardiac enlargement noted on a routine examination led to further studies, hypothyroidism and "myxedema heart" were diagnosed. With thyroid replacement therapy the patient made dramatic recovery and the heart size returned to normal.

GENERIC AND TRADE NAME OF DRUG

Chlordiazepoxide hydrochloride—*Librium*®

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